REMARKS

Reconsideration and allowance are respectfully requested.

Claims 1-2, 4-12, 14-26 and 28-30 are pending. Applicants note that the Office Action Summary contains an incorrect "Disposition of Claims": claims 1-24 (not claims 1-20) were rejected and claims 25-30 (not claims 21-30) were withdrawn from consideration. Rejoinder of non-elected claims is requested upon an indication that an elected claim is allowable.

The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. The independent claims are amended to specify that the core contains "an alkaline additive" and the hydrophobic wax of the release-controlling coating is "20 to 35 wt%, based on the weight of the release-controlling coating" (see claims 1, 25 and 30). Support for these amendments can be found at page 14, lines 10-12, and page 19, lines 1-4, of the specification. The limitations of claims 3, 13 and 27 are redundant in view of the present amendments. Thus, they were canceled.

Claim 22 was objected to. In view of its amendment, withdrawal of the objection is requested.

It was alleged on page 4 of the Office Action that a certified copy of the Japanese priority application was not received by the USPTO. Applicants provided a certified copy to the Receiving Office under PCT Rule 17 and the International Bureau should forward a copy to each of the designated offices. Attached is a copy of the Notification acknowledging that the priority document was received by the International Bureau. See also M.P.E.P. § 1893.03(c). Therefore, in accordance with M.P.E.P. § 1896 III, the Examiner is respectfully requested to consult with the Special Program Examiner in his Technology Center to obtain a certified copy of the priority document. Also see PCT Rule 17.2 which states, "No such Office shall ask the applicant himself to furnish it with a copy."

35 U.S.C. 112 – Definiteness

Claims 21-24 were rejected under Section 112, second paragraph, as allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse because their specification and

the present amendments clarify the relationship of the composition, package, as those terms are used to describe the claimed invention.

The "the controlled-release pharmaceutical composition" and "enteric pharmaceutical composition in which a core containing an acid-unstable physiologically active substance is covered with an enteric coating" are not duplicative. The first controlled-release pharmaceutical composition according to claim 1 is comprised of a release-controlling coating containing an enteric polymer. The second enteric pharmaceutical composition is comprised of an enteric coating. Both also have a core containing an acid-unstable physiologically active substance, but the two compositions are not identical and duplicative. For example, the first composition requires a disintegrant and an alkaline additive; they are not required components of the second composition. And by contrast, the coating of the second composition does not necessarily contain water-insoluble polymer, enteric polymer, and hydrophobic wax as required by the first composition's coating. The two compositions are not necessarily duplicative as alleged in the Office Action.

For the convenience of the Examiner, it is noted that production of the claimed products (i.e., the covering of a core with a coating) is described on pages 20-22 of Applicants' specification. Use of *composition*, *package*, and *packaging container* on pages 24-26 of the present specification define those terms as recited in the claims.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See id. ("Often, it will be necessary for a court

to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See id. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a prima facie case under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. An inquiry is required as to "whether the improvement is more than the predictable use of prior art elements according to their established functions." Id. at 1396. But a claim that is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Id. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 1-21 were rejected under Section 103(a) as allegedly unpatentable over Aoki et al. (WO 03/43661) in view of Nakajima (JP 2000-128779). Applicants traverse.

AOKI discloses a pharmaceutical composition comprised of (1) a core containing rabeprazole and alkaline additive and (2) a coating containing water-insoluble polymer and enteric polymer, which covers the core. In all of AOKI's examples, the amount of talc, which is a hydrophobic wax, can be calculated to be 7.5 wt% as follows:

$$7.5 / (60 + 20 + 7.5 + 4.5 + 8) \times 100 = 7.5 \text{ wt\%}$$

Although all of the AOKI's examples disclose that talc is present at 7.5 wt% in the release-controlling coating, this amount of talc is usually contained as a lubricant in the coating for a conventional pharmaceutical composition. In addition, nowhere in AOKI is there any teaching or suggestion that the hydrophobic wax in the release-controlling coating containing the water-insoluble substance, enteric polymer, and the hydrophobic wax is contained in an amount which is more than that required for a conventional use as a lubricant.

NAKAJIMA discloses a tablet preparation having a core comprising a drug and a water-swelling substance, which is coated with ethyl cellulose and a water-insoluble

powdered substance. It is described at paragraph [0070] of NAKAJIMA that the time from administration of the medication to initial release of the drug (i.e., the lag time) can be controlled with good reproducibility by adjusting the type and amount of the water-insoluble powdered substance contained in the coating.

But NAKAJIMA's core does not comprise an alkaline additive nor does its coating comprise an enteric polymer. NAKAJIMA is completely silent as to the use of the enteric polymer in the coating which covers the core. Further, there is no recognition in NAKAJIMA of the significance of the numerical limitation of the amount of the hydrophobic wax in a coating containing a water-insoluble, an enteric polymers and a hydrophobic wax, in order to provide a controlled-release pharmaceutical composition which has little variation in dissolution lag time. Therefore, NAKAJIMA does not teach or suggest a reasonable expectation of success to use the water-insoluble powdered substance to control the lag time of Applicants' claimed pharmaceutical composition (i.e., a core containing an acid-unstable physiologically active substance, a disintegrant, and an alkaline additive and a release-controlling coating which covers the core, and which contains a water-insoluble polymer, an enteric polymer, and a hydrophobic wax). There is no evidence provided in the Office Action that NAKAJIMA's coating would control the lag time when used with a core containing an acid-unstable physiologically active substance, a disintegrant, and an alkaline additive.

By contrast, Applicants' claimed invention solves the problem of providing a controlled-release pharmaceutical composition which has little variation in dissolution lag time. There is no teaching or suggestion in AOKI of this problem to be solved by the present invention. In general, the amount of hydrophobic wax was not disclosed to be a result-effective variable for controlled release or any other desirable characteristic of a pharmaceutical composition. Since AOKI does not teach or make obvious the technical relationship between the dissolution lag time in the controlled-release pharmaceutical composition and the amount of the hydrophobic wax in the release-controlling coating containing water-insoluble polymer, enteric polymer, and hydrophobic wax, Applicants submit that one of ordinary skill in the art would not have varied the amount of hydrophobic wax in the coating from reading AOKI and NAKAJIMA to control release of drug

from a core containing an acid-unstable physiologically active substance, a disintegrant, and an alkaline additive.

Claims 22-24 were rejected under Section 103(a) as allegedly unpatentable over Aoki in view of Nakajima as applied above, and further in view of Whittle (U.S. Patent 6,444,689). Applicants traverse.

The failure of AOKI and NAKAJIMA to disclose the claimed invention (see the above explanation why claims 1-21 are not obvious over AOKI in view of NAKAJIMA) is not remedied by the attempt to combine their disclosures with WHITTLE. The Examiner cited WHITTLE for its disclosure of pharmaceutical preparations containing benzimidazole compounds. But Applicants submit that WHITTLE does not provide a reason to use 20 to 35 wt% (based on the weight of the release-controlling coating) of hydrophobic wax in a coating containing water-insoluble polymer, enteric polymer, and hydrophobic wax to control release of drug from a core containing an acid-unstable physiologically active substance, a disintegrant, and an alkaline additive. Since these features of Applicants' claimed invention are sufficient to distinguish over the cited documents, other incorrect allegations about their disclosures are not disputed here. But the opportunity to dispute them in the future is reserved.

Claims 1-21 were rejected under Section 103(a) as allegedly unpatentable over Saeki et al. (U.S. Patent 5,035,899) in view of Aoki et al. (WO 03/43661). Applicants traverse.

SAEKI merely discloses a peroral preparation comprising (1) a core containing rabeprazole and (2) a first layer, coated on the core, comprising a hardly water-soluble, film-forming material and fine particles of a hardly water-soluble substance, suspended in the material; and (3) a second layer, coated on the first layer, of enteric film. But it is is completely silent as to use of a release-controlling coating containing water-insoluble polymer, enteric polymer, and hydrophobic wax, which covers the core.

Applicants' claimed invention is a controlled-release pharmaceutical composition that provides the unexpected result of having little variation in dissolution lag time and percentage of dissolution over time, and high reliability of dissolution characteristics. It is submitted SAEKI and AOKI fail to teach or suggest the claimed pharmaceutical compo-

sition because they do not make obvious using 20 to 35 wt% (based on the weight of the release-controlling coating) of hydrophobic wax to control release of the drug. Accordingly, the above-mentioned remarkable technical effects and advantages which can be obtained from the present invention cannot be reasonably expected in view of the cited documents. Further, Applicants submit that the above-mentioned advantages are neither suggested nor rendered obvious by the cited documents.

Claims 22-24 were rejected under Section 103(a) as allegedly unpatentable over Aoki in view of Nakajima as applied above, and further in view of Chen et al. (U.S. Application 2002/0045184). Applicants traverse.

The failure of AOKI and NAKAJIMA to disclose the claimed invention (see the above explanation why claims 1-21 are not obvious over AOKI in view of NAKAJIMA) is not remedied by the attempt to combine their disclosures with CHEN. The Examiner cited CHEN for its disclosure of a blister card. But Applicants submit that CHEN does not provide a reason to use 20 to 35 wt% (based on the weight of the release-controlling coating) of hydrophobic wax in a coating containing water-insoluble polymer, enteric polymer, and hydrophobic wax to control release of drug from a core containing an acid-unstable physiologically active substance, a disintegrant, and an alkaline additive. Since these features of Applicants' claimed invention are sufficient to distinguish over the cited documents, other incorrect allegations about their disclosures are not disputed here. But the opportunity to dispute them in the future is reserved.

Withdrawal of the Section 103 rejections is requested because the claims would not have been obvious to one of ordinary skill in the art when this invention was made.

Double Patenting

Claims 1-20 were provisionally rejected for statutory double patenting as allegedly claiming the same invention as that of claims 1-20 of copending Application No. 11/543,991. Applicants traverse because claims 1-20 of the '991 application were canceled on March 17, 2009.

Claims 1-20 were provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-3, 5-8 and

10-12 of copending Application No. 10/849,544 in view of Aoki and Nakajima. It was also alleged that claim 1-20 are directed to an invention not patentably distinct from claims 1-3, 5-8 and 10-12 of commonly assigned Application No. 10/849,544. Applicants traverse because, as discussed above for the Section 103 rejections, AOKI and NAKAJIMA do not make obvious using 20 to 35 wt% hydrophobic wax to control release of drug from a core containing an acid-unstable physiologically active substance, a disintegrant, and an alkaline additive with a reasonable expectation of success.

Claims 1-20 were provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 41-43 and 45-55 of copending Application No. 10/938,554 in view of Aoki and Nakajima. It was also alleged that claim 1-20 are directed to an invention not patentably distinct from claims 41-43 and 45-55 of commonly assigned Application No. 10/938,554. Applicants traverse because, as discussed above for the Section 103 rejections, AOKI and NAKAJIMA do not make obvious using 20 to 35 wt% hydrophobic wax to control release of drug from a core containing an acid-unstable physiologically active substance, a disintegrant, and an alkaline additive with a reasonable expectation of success.

Withdrawal of the double patenting rejections is requested for the above reasons.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /Gary R. Tanigawa/
Gary R. Tanigawa
Reg. No. 43,180

901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100